Transmittal Letter to the United States Designated/Elected Office (DO/EO/US)

10/070673

FORM PTO-1390

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Docket No.	**FI-37PCT**
U.S. Application No	
International Application No	**PCT/EP00/08647**
International Filing Date.	**September 5, 2000**
Priority Dates Claimed	**September 6, 1999**
Title of Invention	**COMPOSITION FOR STIMULATING INTESTINAL ACTIVITY AND PROCESS FOR ITS PREPARATION**
Applicant(s) for (DO/EO/US)	**Günther Beisel**

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. X This is a FIRST submission of items concerning a filing under 35 U S C 371.
2. ___ This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C 371
3. X This express request to begin national examination procedures 35 U S C 371 (f) at any time rather than delay examination until the expiration of the applicable time limit set forth in 35 U S C 371(b) and PCT Articles 22 and 39(1)
4. ___ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date
5. X A copy of the International Application as filed [35 U.S C 371(c)(2)].
   a) X is transmitted herewith (required only if not transmitted by the International Bureau)
   b) ___ has been transmitted by the international Bureau.
   c) ___ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. X A translation of the International Application into English [35 U S C.371(c)(2)]
7. ___ Amendments to the claims of the International Application under PCT Article 19 [35 U S C 371(c)(3)]
   a) ___ are transmitted herewith (required only if not transmitted by the International Bureau)
   b) ___ have been transmitted by the International Bureau
   c) ___ have not been made, however, the time limit for making such amendments has NOT expired
   d) ___ have not been made and will not be made
8. ___ A translation of the amendments to the claims under PCT Article 19 [35 U S C 371(c)(3)].
9. X An oath or declaration of the inventor(s) [35 U.S.C.371(c)(4)]. UNSIGNED
10. ___ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 [35 U S C 371(c)(5)]

Items 11. to 16. below concern other document(s) or information included:

11. X An Information Disclosure Statement under 37 C.F.R. 1 97 and 198
12. ___ An Assignment document for recording A separate cover sheet in compliance with 37 CFR 3 28 and 3.31 is included
13. X A FIRST preliminary amendment
    ___ A SECOND or SUBSEQUENT preliminary amendment
14. ___ A substitute specification.
15. ___ A change of power of attorney and/or address letter
16. X (other items or information) PTO-1449 w/ 6 references and International Search Report

EXPRESS MAIL No.: EU 076 175 262 US Deposited. March 6, 2002

I hereby certify that this correspondence is being deposited with the United States Postal Service Express mail under 37 CFR 1 10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, DC 20231.

Friedrich Kueffner

March 6, 2002
Date

[redacted]

U.S. Application No (if known, see 37 C F R. 1 50): 10/070673
International Application No . PCT/EP00/08647

Docket No FI-37PCT

17. X The following fees are submitted

BASIC NATIONAL FEE [37 CFR 1.492(a)(1)-(5)]:		CALCULATIONS	PTO USE ONLY
X Search Report has been prepared by the EPO or JPO	$ 890.00		
___ International preliminary examination fee paid to USPTO [37 CFR 1 482]	$ 710.00		
___ No International preliminary examination fee paid to USPTO [37 CFR 1 482] but International search fee paid to USPTO [37CFR 1.445(a)(2).....	$ 740.00		
___ Neither International preliminary examination fee [37 CFR 1 482] nor International search fee [37 CFR 1 445(a)(2]) paid to USPTO:	$ 1040.00		
___ International preliminary examination fee paid to USPTO [37 CFR 1.482] and all claims satisfied provisions of PCT Article 33 (2) to (4).....	$ 100.00		
ENTER APPROPRIATE BASIC FEE AMOUNT:		$ 890.00	
Surcharge of $ 130 00 for furnishing the oath or declaration later than ___20 ___30 months from the earliest claimed priority date [37 CFR 1 492(e)]		$	

Claims	filed	Extra	Rate	
Total Claims	16	-20=	x $ 18 =	$
Indep Claims	1	- 3=	x $ 84 =	$
Multiple Dependent Claims (if applicable)			+ $ 280 =	$

TOTAL OF ABOVE CALCULATIONS:	$ 890.00	
Small Entity Status is claimed (divided by 2)	445.00	
SUBTOTAL:	$ 445.00	
Processing fee of $ 130 00 for furnishing the English translation later than ___20 ___30 months from the earliest claimed priority date [37 CFR 1 492(f)]	$	
TOTAL NATIONAL FEE:	$ 445.00	
Fee for recording the enclosed assignment [37 CFR 1.21(h)] The assignment must be accompanied by an appropriate cover sheet [37 CFR 3 28,3 31] $ 40.00 per property	$	
TOTAL FEES ENCLOSED:	$ 445.00	
AMOUNT TO BE REFUNDED:	Refunded	$
AMOUNT TO BE CHARGED:	Charged	$

a) X A check in the amount of **$ 445.00** to cover the above fees is enclosed.

b) _ Please charge my Deposit Account No 11-1835 in the amount of $ to cover the above fees. A duplicate copy of this sheet is enclosed

c) X The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No **11-1835** A duplicate copy of this sheet is enclosed

NOTE: Where an appropriate time limit under 36 CFR 1 494 or 1 495 has not been met, a petition to revive [37 CFR 1 137(a) or (b)] must be filed and granted to restore the application to pending status

SEND ALL CORRESPONDENCE TO:
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signature

29,482
Reg. No.

March 6, 2002
Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

FI-37PCT

Applicant(s)	:	Günther Beisel
Serial No.	:	NOT YET KNOWN (PCT/EP00/08647)
Int. Filed	:	September 5, 2000
For	:	COMPOSITION FOR STIMULATING INTESTINAL ACTIVITY AND PROCESS FOR ITS PREPARATION

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

S I R:

In advance of the first office action, please amend the claims as follows:

IN THE CLAIMS

Replace current claims 1 - 16 by the enclosed amended claims 1 - 16. A marked-up version of amended claims 1 - 16 is also enclosed.

REMARKS

Claims 1 - 16 are in the application.

As a result of the foregoing amendment, the claims have been amended to remove improper multiple dependencies.

Any additional fees or charges required at this time in connection with the application may be charged to our Patent and Trademark Office Deposit Account No. 11-1835.

Respectfully submitted,

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March 6, 2002
FK:ml
ENCLS:
Amended Claims;
Marked-Up Version.

EXPRESS MAIL No.: **EU 076 175 262 US** Deposited: **March 6, 2002**

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Friedrich Kueffner

CLEAN VERSION OF AMENDED CLAIMS

1. A composition for stimulating intestinal activity and/or improving and/or normalizing bowel movements comprising a material in the form of a sponge-like structure, wherein it has 3-dimensional polymeric networks and, if the material is degradable in the stomach and/or small intestine, is provided with a compound which is only soluble in the intestine.

2. The composition as claimed in claim 1, wherein the sponge-like structure is coated with the compound.

3. The composition as claimed in claim 1, wherein the sponge-like structure is introduced into a container which consists of a compound which is exclusively soluble in the intestine.

4. The composition as claimed in claim 1, wherein the compound is introduced into the sponge-like structure.

5. The composition as claimed in claim 1, wherein the compound is soluble in liquids having a pH of 5 to 10.

6. The composition as claimed in claim 1, wherein the compound is soluble in liquids having a pH of 5.5 to 8.5.

7. The composition as claimed in claim 1, wherein the compound is soluble in liquids having a pH of 6.4 ± 0.6 to 7.0 ± 0.7.

8. The composition as claimed in claim 1, wherein the sponge-like structure comprises natural, semisynthetic or synthetic polymers and stably crosslinked bodies or combinations thereof.

9. The composition as claimed in claim 1, wherein the sponge-like structure comprises collagen, cellulose or alginate.

10. The composition as claimed in claim 1, wherein the sponge-like structure is compressible to half to one hundredth of its original size, preferably one quarter to one fiftieth, particularly preferably to one tenth to one twentieth.

11. The composition as claimed in claim 1, wherein the material can be decompressed in the intestine to two to one hundred times its size in the compressed state, preferably four to fifty times, particularly preferably to ten to twenty times.

12. The composition as claimed in claim 1 for use for stimulating intestinal activity and for improving and/or normalizing bowel movements comprising a material in the form of a sponge-like

structure, wherein it has 3-dimensional polymeric networks and, if the material is degradable in the stomach and/or small intestine, is provided with a compound which is only soluble in the intestine.

13. A process for preparing a composition for stimulating intestinal activity as claimed in claim 1, wherein a material in the form of a sponge-like structure is reversibly compressed and, if appropriate, a compound is applied to this structure and/or such a compound is introduced into the sponge-like structure and/or this structure is coated with such a compound.

14. The use of the composition as claimed in claim 1 for preparing compositions for stimulating intestinal activity and for improving and/or normalizing bowel movements.

15. The use of the composition as claimed in claim 1 for preparing pharmaceutically active compositions and/or foodstuffs and/or food supplements and/or (dietetic) foods.

16. The use of the composition as claimed in claim 1 for stimulating intestinal activity and/or for improving and/or normalizing bowel movements and/or shortening the transit time of the chyme in the intestine, combined with a laxative action.

MARKED-UP VERSION OF AMENDED CLAIMS

1. A composition for stimulating intestinal activity and/or improving and/or normalizing bowel movements comprising a material in the form of a sponge-like structure, [characterized in that] wherein it has 3-dimensional polymeric networks and, if the material is degradable in the stomach and/or small intestine, is provided with a compound which is only soluble in the intestine.

2. The composition as claimed in claim 1, [characterized in that] wherein the sponge-like structure is coated with the compound.

3. The composition as claimed in [either claim 1 or 2, characterized in that] claim 1, wherein the sponge-like structure is introduced into a container which consists of a compound which is exclusively soluble in the intestine.

4. The composition as claimed in [one of claims 1 to 3, characterized in that] claim 1, wherein the compound is introduced into the sponge-like structure.

5. The composition as claimed in [one of claims 1 to 4, characterized in that] claim 1, wherein the compound is soluble in liquids having a pH of 5 to 10.

6. The composition as claimed in [one of claims 1 to 5, characterized in that] claim 1, wherein the compound is soluble in liquids having a pH of 5.5 to 8.5.

7. The composition as claimed in [one of claims 1 to 6, characterized in that] claim 1, wherein the compound is soluble in liquids having a pH of 6.4 ± 0.6 to 7.0 ± 0.7.

8. The composition as claimed in [one of claims 1 to 7, characterized in that] claim 1, wherein the sponge-like structure comprises natural, semisynthetic or synthetic polymers and stably crosslinked bodies or combinations thereof.

9. The composition as claimed in [one of claims 1 to 8, characterized in that] claim 1, wherein the sponge-like structure comprises collagen, cellulose or alginate.

10. The composition as claimed in [one of claims 1 to 9, characterized in that] claim 1, wherein the sponge-like structure is compressible to half to one hundredth of its original size, preferably one quarter to one fiftieth, particularly preferably to one tenth to one twentieth.

11. The composition as claimed in [one of claims 1 to 10, characterized in that] claim 1, wherein the material can be decompressed in the intestine to two to one hundred times its size in the compressed state, preferably four to fifty times, particularly preferably to ten to twenty times.

12. The composition as claimed in [one of the preceding claims] claim 1 for use for stimulating intestinal activity and for improving and/or normalizing bowel movements comprising a material in the form of a sponge-like structure, [characterized in that] wherein it has 3-dimensional polymeric networks and, if the material is degradable in the stomach and/or small intestine, is provided with a compound which is only soluble in the intestine.

13. A process for preparing a composition for stimulating intestinal activity as claimed in [one of claims 1 to 12, characterized in that] claim 1, wherein a material in the form of a sponge-like structure is reversibly compressed and, if appropriate, a compound is applied to this structure and/or such a compound is introduced into the sponge-like structure and/or this structure is coated with such a compound.

14. The use of the composition as claimed in [one of the preceding claims] claim 1 for preparing compositions for stimulating intestinal activity and for improving and/or normalizing bowel movements.

15. The use of the composition as claimed in [one of the preceding claims] claim 1 for preparing pharmaceutically active compositions and/or foodstuffs and/or food supplements and/or (dietetic) foods.

16. The use of the composition as claimed in [one of the preceding claims] claim 1 for stimulating intestinal activity and/or for improving and/or normalizing bowel movements and/or shortening the transit time of the chyme in the intestine, combined with a laxative action.

Composition for stimulating intestinal activity and process for its preparation

The present invention relates to a composition for stimulating intestinal activity and/or for improving and/or normalizing bowel movements.

US 3,688,763 describes a method of collecting cellular material from the large intestine of a patient. The patient swallows a capsule, the outer coating of which together with the container situated underneath dissolves in the intestine and releases a compressed sponge which is then expelled via natural evacuation of the bowels.

On its transport through the intestine, the sponge scrapes off outer cells of the intestinal lumen which are carried along to the outside. By this means, in a simple manner, intestinal cells are removed from the patients with the purpose of then studying these for tumors or cancer cells.

This system had the object of collecting intestinal cells for analytical purposes. However, targeted stimulation of intestinal activity is not achieved in this manner.

DE 4 025 912 discloses a composition for oral intake which consists of a receptacle which, in the stomach, can be dissolved and releases the contents. This receptacle is filled with a material which on being released in the stomach increases in volume and as a result induces in the person a feeling of satiation.

The disadvantage of this system is that it is directed solely toward filling the stomach. A stimulation of intestinal activity is thus not associated with it, however.

It is an object of the present invention to provide a composition comprising a material in the form of a sponge-like structure which is deformable, shape-reducible and/or reversibly compressible, passes through the esophagus and the stomach and in the intestine develops a stimulating action on the intestinal activity.

This object is achieved by means of the fact that the sponge-like structure predominantly has three-dimensional polymeric networks and, if the material is degradable in the stomach and/or small intestine, is provided with a compound which is only soluble in the intestine.

The dissolution of the compound is affected in this case by various parameters, in part also prevailing simultaneously in the intestine, for example pH, pressure, redox potential and enzymatic dissolution via the intestinal flora. In addition, the residence time of the composition in the intestine also affects the rate at which the compound dissolves.

For preference, the compound dissolves at a pH between 5 and 10, preferably between 7 and 9, particularly preferably between 5.5 and 8.5. Dissolution in the pH environment of the intestine at a pH between 6.4 ± 0.6 and 7.0 ± 0.7 is most preferred. In particular, those compounds are suitable which dissolve depending on the redox potential, enzymatic activities and pressure.

The compound is applied to the sponge-like structure according to the invention preferably in the form of a coating which, if appropriate, can also be made up of a plurality of layers. The minimum layer thickness here can vary considerably and is dependent on the film-former used and its composition. Osterwald H. et al.

(Acta Pharm Technol, 1980, 26: 201-209) describes, for example, a minimum layer thickness of 46 µm for the preparation of a film-former in organic solvents, preparation with an ammonium salt solution requires a layer thickness of 161 µm, as an emulsion 46 µm and as a latex dispersion 52 µm. According to the invention, the layer thickness is from 10 µm to several millimeters, preferably from 15 µm to 3 mm.

However, instead of a coating applied directly to the structure, the sponge-like structure can also be introduced into a container which dissolves under the above-described conditions. That is to say the container is stable in the stomach, but dissolves in the intestine.

In another variant of the invention, the compound can be introduced into the sponge-like structure. This may be achieved, for example, by mixing the material with the compound as early as when the sponge-like structure is prepared. Preferably, this may also be achieved by impregnating the material in a solution of the compound. Obviously, such a structure can also be additionally provided with a coating of the compound. Equally, the impregnated structure can also be introduced into the above-described container. In addition, the structure can be introduced into a container which itself is coated or impregnated with the compound or into which the compound is introduced.

The time and location of the dissolution of the compound may be influenced by the selection and combination of the compounds, which results in targeted release of the sponge-like structure in the intestine and, in particular, in the various intestinal sections, such as the jejunum, ileum and colon. The solubility of the compounds can depend on one or more factors, for example pH, time of exposure, redox potential of the

intestine, enzymatic activities of the intestinal flora, or pressure which is produced by intestinal peristalsis. The various possibilities for controlling the release of active compounds are described extensively. The pH-dependent solubility is described, for example, in *Marvola et al.*, Eur J Pharm Sci, 1999, 7:259-267 and *Khan Zl et al.*, J Controlled Release, 1999, 58:215-222. *Pozzi F. et al.*, J Controlled Release, 1994, 31:99-108; *Wilding IR et al.*, Pharmacol Ther, 1994, 62:97-124; *Niwa K. et al*, J Drug Target, 1995, 3:83-89 and US-4871549 disclose systems which release the active compounds as a function of time. Examples of systems having a combined pH and time dependency are described in *Rodriguez M.et al.*, J Controlled Release, 1998, 55:67-77 and *Gazzinga A. et al.*, STP Pharm Sci, 1995, 5:83-88. The dissolution of compounds due to changed redox potential in the intestine is dealt with by *Bronsted H. et al.*, Pharm Res 1992, 9:1540-1545; *Yeh PY et al.*, J Controlled Release, 1995, 36:109-124; *Shanta KL et al.*, Biomaterials, 1995, 16:1313-1318 and *Kimura Y et al.*, Polymer, 1992, 33:5294-5299. Examples of systems which are released by the enzymes of the intestinal flora are described in *Ashford M et al.*, J Controlled Release, 1994, 30:225-232; *Fernandez-Hervas MJ et al.*, Int J Pharm, 1998, 169:115-119; *EP-0460921; US-4432966* and *Milojevic S et al.*, J Controlled Release, 1996, 38:75-84. The dissolution of systems due to the pressure of intestinal peristalsis is covered in *Muraoka M et al.*, J Controlled Release, 1998, 52:119-129.

Preference is given according to the invention to the following compounds and their combinations which are, however, in no way limiting for the present invention:

hydroxypropyl methyl cellulose phthalate (HPMCP 55), hydroxypropyl methyl cellulose acetate succinate (Aqoat AS-MF, Aqoat AS-HF), 1:1 copolymer of methacrylic acid

and ethyl acrylate (Eudragit®L), copolymer of vinyl acetate and crotonic acid (Coating CE 5142), cellulose acetate phthalate (CAP, Aquateric), methacrylate copolymers (Eudragit®S), shellac, Time Clock System®, carnauba wax, hydroxypropyl methyl cellulose (TC-5), Pulsincap®, polyethylene glycol, crosslinked polyethylene glycol, ethyl cellulose, ethyl cellulose/ethanol mixture, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, glycerol monostearate, Eudragit®E. In addition, hydrogels from azo compounds are possible, for example N-substituted methacrylamide, N-tert-butylacrylamide, acrylic acid in the presence of 4,4'-bis(methacryloylamino)azobenzene, 4,4'-bis(N-methacryloyl-6-aminohexanoylamino)azobenzene or 3,3',5,5'-tetrabromo-4,4,4'4'-tetra(methacryloylamino)azobenzene. Examples of other compounds are unbranched polymer precursors, for example containing N,N-dimethylacrylamide, N-tertbutylacrylamide, acrylic acid, N-methacryloylglycylglycine p-nitrophenyl ester, crosslinked by suitable crosslinkers, for example N,N'-(ω-aminocaproyl)-4,4'-diaminoazobenzene and polymers containing azo compounds, for example 2-hydroxyethyl methacrylate, 4-(methacryloyloxy)azobenzene, N-(2-hydroxypropyl)methacrylamide copolymers, copolymers containing styrene and 2-hydroxyethylmethacrylate crosslinked by, for example, 4,4'-divinylazobenzene or N,N'-bis(β-sterylsulfonyl)-4,4'-diaminoazobenzene. Also, poly(ether-ester)azo polymers can be used according to the invention, for example copolymers containing 4-[4-[(6-hydroxyhexyl)-oxy]phenyl]azobenzoic acid and 16-hydroxyhexadecanoic acid, copolymers containing 4-[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]benzoic acid, 4-[4-[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]phenyl]azobenzoic acid and 16-hydroxyhexadecanoic acid or 12-hydroxydodecanoic acid and segmented polyurethanes containing m-xylene diisocyanate, 3,3'-dihydroxyazobenzene, polyethylene glycol or 1,2-propanediol. In addition, usable

compounds are azo-compound-containing polyamides or copolymers of 4-[4-(chlorocarbonyl)phenyl)]azobenzoyl chloride and α,ω-bis(aminopropyl)poly(tetramethylene oxide) and copolymers of 4-[4-chlorocarbonyl)-phenyl]azobenzoyl chloride and Jeffamine ED-600.

In addition, pectins are used, which can be additionally coated or embedded in a matrix, for example, methoxy pectin, amidated pectin, calcium pectinate, pectin in combination with ethyl cellulose (Aquacoat, Surelease), acrylic ester polymers (Eudragit RS30D, Eudragit NE30D). In addition, combinations of pectins with other dietary fibers are used. Examples of dietary fibers are guar (galactomannan) or chitosan, the dietary fibers themselves in turn being able to be coated or be a constituent of a matrix. In this case, the following substances are used as film-formers: polymethacrylate solutions, copolymers containing polyurethane and di-, oligo- or polysaccharides (galactomannans) and ethyl-galactomannans or acetylgalactomannans. In addition, cyanoacrylate, inulin, inulin suspensions containing Eudragit-RS, methacrylated inulin, chondroitin sulfate, chondroitin polymers containing 1,12-diaminododecane and dicyclohexylcarbodiimide, amorphous amylose or amorphous amylose together with other film-forming polymers are used as film-formers. In addition, dextrans can be used which can be crosslinked in various ways, for example with diisocyanates, fatty acid esters, for example lauric acid, glutaraldehyde. Conjugates of biphenylacetic acid and β-cyclodextrin, films of β-cyclodextrins with methacrylic acid copolymers or acrylic acid polymers with disaccharide side groups are also used according to the invention.

The choice of compounds and their many possible combinations make targeted release of the sponge-like structure in the intestine possible.

In addition, the present invention relates to a composition for use for stimulating intestinal activity and for improving and/or normalizing bowel movements comprising a material in the form of a sponge-like structure which has 3-dimensional polymeric networks and, if the material is degradable in the stomach and/or small intestine, is provided with a compound which is only soluble in the intestine.

Sponge-like structures are taken to mean according to the invention foams which consist of gas-filled spherical/polyhedral cells which are limited by highly viscous or solid cell walls. It is possible to employ according to the invention both naturally occurring sponges and synthetically prepared sponge-like structures.

The sponge-like or spongy structures are prepared by methods known per se from the prior art. Depending on the starting material employed, in the simplest case a foam can be obtained by blowing, beating, shaking, spraying or stirring in the relevant gas atmosphere. In the case of polymers, the foam structure is produced by chemical reactions. Thus polyurethanes are foamed by adding blowing agents which decompose at a defined temperature during processing with gas formation, or by adding liquid solvents during the polymerization. Foaming takes place either on leaving the extrusion die, that is to say following the extrusion or injection molding, or in open molds. Curing takes place under the conditions characteristic of the particular chemical compound of the material.

An essential prerequisite for the employability of the material is that it is compressible without breaking the cell walls. It is further essential for the selection of material and manner of foam formation that

it remains swellable without the cell walls being destroyed.

In order to prevent constipation of the intestine or, in the worst case, even an intestinal obstruction, the volume of the decompressed sponge-like structures must be chosen appropriately. In order to achieve the desired stimulating effect on the intestinal activity even with relatively small sponge-like structures, a plurality of inventive compositions can be taken orally.

The sponge-like structure can have any desired shape and size in the decompressed state. However, preference is given to cuboid or rectangular or round embodiments.

Preferably, the material is designed in such a manner that the sponge-like structure can be compressed to 1/2 to 1/100, preferably 1/4 to 1/50, particularly preferably 1/10 to 1/20, of its volume or its size. Under physiological conditions, the compressed material, after passage through the esophagus and the stomach, is to be able to expand preferably to two to one hundred times, particularly preferably to four to fifty times, very particularly preferably to ten to twenty times, its volume in the intestine.

For the sponge-like structure, it is possible to employ according to the invention natural, semisynthetic or synthetic polymers. Examples of suitable synthetic polymers are polyurethanes, polyacrylates, poly(meth)acrylic esters, and homopolymers and copolymers of vinyl acetate. The natural and semisynthetic polymers include, inter alia, cellulose, cellulose ethers, diethylcellulose or cellulose esters, such as cellulose diacetate, cellulose triacetate, cellulose acetate propionate, cellulose acetate and cellulose butyrate. Those which are suitable according

to the invention are, for example, cellulose derivatives, in particular corresponding ethers, for example methyl cellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, or sodium carboxymethyl cellulose (preferably those compounds of relatively high viscosity); natural (anionic) mucilages, for example xanthan gum, guar gum, tragacanth or alginic acid and salts thereof, and the like. In addition, the use of insoluble polysaccharides such as chitin or chitin derivatives or microcrystalline cellulose is also conceivable. Particular preference is given according to the invention to unbranched high-molecular-weight polymers. In particular, those polymers can be employed according to the invention which have a fibrous structure. Examples of such materials are the scleroproteins such as keratins, conchagens, fibroin, elastins and collagen.

Also, polymers which are crosslinked in a stable manner come into consideration. In particular, uronic-acid-containing polysaccharides or their salts are conceivable here that are crosslinked to one another by ionic bonds and are crosslinked in a stable manner by additional covalent bonds, for example by ester bonds catalyzed by mineral acids.

In a particular embodiment of the invention, the polymers can also decompress as early as in the stomach and pass into the intestine in this state and pass through the latter. Materials in the form of a sponge-like structure which come into consideration here are, in particular, those which are scarcely noticeably degradable or absorbable, to not at all degradable or absorbable, in the gastrointestinal fluids.

The present invention further relates to a process for preparing the above-described composition. In the process, in principle, first a suspension of the materials for the sponge-like structure is prepared and

then freeze-dried. If appropriate, the material for the sponge-like structure is, in advance, comminuted and/or subjected to an alkaline and/or an acid pretreatment. The freeze-drying is preferably carried out at -80 to +50°C, in particular at -30 to +40°C.

The resultant material is then compressed. This can be achieved by pressing, rolling or comparable methods. In a particular embodiment of the invention, compression of the material can also be achieved by chewing movements during the oral intake of the material.

The sponge-like compressed structure thus prepared can, in a preferred embodiment of the invention, be provided with the above-described compound. That is to say, either a container, for example a capsule casing, is produced from the compound and the sponge-like structure is introduced into this. Or, the compound is applied directly to the structure, for instance by impregnation, spraying, spreading or similar methods.
In another embodiment of the invention, the compound is introduced into the sponge-like structure. This can be achieved, for example, by impregnation.
In addition, it is conceivable that the compound is introduced into the sponge-like structure as early as during the preparation of the material by direct mixing of material and compound.

It is a purpose of the inventive process to obtain a composition which is present in the intestine in decompressed form and thus exerts a stimulating action on the intestinal activity. This purpose is achieved by said process steps.
In contrast to other foodstuff/food supplement/dietetic or medicinal products which are decomposed rapidly in the intestine or even pass into the intestine in a comminuted state, the sponge or foam body, which consists of natural, semisynthetic or synthetic or

stably crosslinked polymers and is prepared in the manner described, retains its original form over several hours due to its predominantly three-dimensional polymeric network. The inventive composition thus exerts, in the intestine, an action which is comparable to that of a dietary fiber and on account of which the intestinal activity is stimulated. In this case, the inventive composition, on passage through the esophagus and during passage through the stomach or small intestine, is present in sufficiently compressed form in order to decompress and develop the desired action in the intestine, in particular in the large intestine.

In a particular embodiment of the invention, the composition, however, can also decompress as early as in the stomach and in this state can pass into the intestine and pass through it. This applies in particular to materials which can also pass through the stomach and small intestine in decompressed form without being degraded.

For the particular case that the material, however, should begin to degrade as early as in the stomach or small intestine, appropriate protection from premature degradation must take place. Such a protection can be achieved by providing the material with a compound which dissolves exclusively in the intestine. In this case, this compound can be incorporated/applied into/onto the material in the manner mentioned above or be coated therewith.

Otherwise, it is, however, perfectly conceivable that the inventive composition can be provided, so to speak optionally, with an above-described compound.

A compound, which may be applied/introduced onto/into the structure, or a coating thereof, firstly gives the

possibility of protecting the material against premature degradation, and secondly gives the possibility of affecting the site of decompression of the material.

The composition which is decompressed according to the invention in the intestine excites the stretch receptors of the intestinal wall, which themselves trigger the contractions of the intestine. This causes the desired stimulation of intestinal activity and results in a shortening of the transit time of the intestinal contents.

In one embodiment of the inventive process which describes the invention in more detail, but does not limit it thereto, the sponge-like structure used can be soluble collagen from the hides of young animals, in particular cattle or pigs. This is because the soluble collagen fractions in the hide of animals become increasingly smaller with increasing age of the organism, since the collagen forms an insoluble three-dimensional network due to intermolecular crosslinking. The crosslinking points are fixed chemical bonds between individual collagen molecules.

In the production of the required collagen suspensions for sponge preparation, therefore, the hides must originate from animals (bulls) which are 1 to 2 years old. Here, the collagen is already forming an insoluble network. Strongly alkaline and acidic pretreatment of the hide, and mechanical forces during production of the sponge suspension, can cause individual chemical and physical crosslinking points in the collagen to be disrupted.

When the sponge is dried by freeze-drying and subsequent heating at 90°C to 130°C, preferably 120°C, new crosslinking points are introduced back into the

sponge material owing to the relatively high temperatures.

This causes a long-lasting insolubility of the sponge body in gastrointestinal fluids and/or water. This relative insolubility is a prerequisite for a relatively strong and stable structure which triggers a long-lasting stimulating effect and thus a laxative (purgative) effect in the intestine.

In a preferred embodiment of the present invention, to prepare the sponge-like structures, stably crosslinked polyuronic-acid-containing polysaccharides are used. Particular preference is given to alginates or their salts. The polymers, in addition to ionic bonds, are additionally stably crosslinked to one another by covalent bonds, in particular by ester bonds which are catalyzed by mineral acid.

The invention is not restricted to the described processes, but also applies to all other processes in which sponges, sponge-like structures or gels are prepared which, owing to the relative insolubility in water and/or gastrointestinal fluids, if appropriate supported by correspondingly suitable compounds, are to achieve or can achieve a long-lasting stimulation of intestinal activity.

The composition according to the invention is taken orally. The compressed sponge body or solid foam body passes through the mouth, throat, esophagus and, if appropriate stomach, by addition of beverage, and gentle chewing or swallowing movements, and swells again in the intestine, preferably to its original volume. If appropriate, the volume can also be greater than or less than the original volume.

Oral intake of the inventive composition results in the stretch receptors in the intestine being excited, since the compressed sponge body or solid foam body, owing to the only slight solubility in the intestine, retains a strong and mechanically stable structure. As a result, long-term excitation of the intestinal activity may be achieved, combined with an improved waterbinding capacity of the stools, followed by more favorable growth conditions of the intestinal flora, as a result of which, finally, intestinal secretion and intestinal blood circulation are excited.

Therefore, the inventive composition is used to stimulate the digestion/intestinal activity, to improve and/or normalize bowel movements, and to shorten the transit time of the chyme in the intestine, combined with a laxative (purgative) effect. Also, the composition can alternatively be used in the fields of pharmacy and/or health, preferably (dietetic) nutrition or food supplementation.

The present invention thus relates, in addition, to the use of the inventive composition for preparing compositions for stimulating intestinal activity and for improving and/or normalizing bowel movements and for preparing pharmaceutically active compositions and/or foodstuffs and/or food supplements and/or dietetic foods.

Patent claims:

1. A composition for stimulating intestinal activity and/or improving and/or normalizing bowel movements comprising a material in the form of a sponge-like structure, characterized in that it has 3-dimensional polymeric networks and, if the material is degradable in the stomach and/or small intestine, is provided with a compound which is only soluble in the intestine.

2. The composition as claimed in claim 1, characterized in that the sponge-like structure is coated with the compound.

3. The composition as claimed in either claim 1 or 2, characterized in that the sponge-like structure is introduced into a container which consists of a compound which is exclusively soluble in the intestine.

4. The composition as claimed in one of claims 1 to 3, characterized in that the compound is introduced into the sponge-like structure.

5. The composition as claimed in one of claims 1 to 4, characterized in that the compound is soluble in liquids having a pH of 5 to 10.

6. The composition as claimed in one of claims 1 to 5, characterized in that the compound is soluble in liquids having a pH of 5.5 to 8.5.

7. The composition as claimed in one of claims 1 to 6, characterized in that the compound is soluble in liquids having a pH of 6.4 ± 0.6 to 7.0 ± 0.7.

8. The composition as claimed in one of claims 1 to 7, characterized in that the sponge-like structure

comprises natural, semisynthetic or synthetic polymers and stably crosslinked bodies or combinations thereof.

9. The composition as claimed in one of claims 1 to 8, characterized in that the sponge-like structure comprises collagen, cellulose or alginate.

10. The composition as claimed in one of claims 1 to 9, characterized in that the sponge-like structure is compressible to half to one hundredth of its original size, preferably one quarter to one fiftieth, particularly preferably to one tenth to one twentieth.

11. The composition as claimed in one of claims 1 to 10, characterized in that the material can be decompressed in the intestine to two to one hundred times its size in the compressed state, preferably four to fifty times, particularly preferably to ten to twenty times.

12. The composition as claimed in one of the preceding claims for use for stimulating intestinal activity and for improving and/or normalizing bowel movements comprising a material in the form of a sponge-like structure, characterized in that it has 3-dimensional polymeric networks and, if the material is degradable in the stomach and/or small intestine, is provided with a compound which is only soluble in the intestine.

13. A process for preparing a composition for stimulating intestinal activity as claimed in one of claims 1 to 12, characterized in that a material in the form of a sponge-like structure is reversibly compressed and, if appropriate, a compound is applied to this structure and/or such a compound is introduced into the sponge-like structure and/or this structure is coated with such a compound.

14. The use of the composition as claimed in one of the preceding claims for preparing compositions for stimulating intestinal activity and for improving and/or normalizing bowel movements.

15. The use of the composition as claimed in one of the preceding claims for preparing pharmaceutically active compositions and/or foodstuffs and/or food supplements and/or (dietetic) foods.

16. The use of the composition as claimed in one of the preceding claims for stimulating intestinal activity and/or for improving and/or normalizing bowel movements and/or shortening the transit time of the chyme in the intestine, combined with a laxative action.

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

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— *Vor Ablauf der für Änderungen der Ansprüche geltenden Frist; Veröffentlichung wird wiederholt, falls Änderungen eintreffen.*

Zur Erklärung der Zweibuchstaben-Codes, und der anderen Abkürzungen wird auf die Erklärungen ("Guidance Notes on Codes and Abbreviations") am Anfang jeder regulären Ausgabe der PCT-Gazette verwiesen.

(54) Title: AGENT FOR STIMULATING BOWEL FUNCTION AND METHOD FOR PRODUCING THE SAME

(54) Bezeichnung: MITTEL ZUR STIMULANZ DER DARMTÄTIGKEIT SOWIE VERFAHREN ZU DESSEN HERSTELLUNG

(57) Abstract: The invention relates to an agent for stimulating bowel function and/or for improving and/or normalizing the action of the bowels. The inventive agent contains a material in the form of a spongy structure that comprises three-dimensional polymer meshes. Said structure is provided with a compound that is exclusively soluble in the intestines, if the material can be decomposed in the stomach and/or the small intestine. The invention further relates to a method for producing such an agent and to the use thereof.

(57) Zusammenfassung: Die vorliegende Erfindung betrifft ein Mittel zur Stimulanz der Darmtätigkeit und/oder zur Verbesserung und/oder Normalisierung des Stuhlgangs, enthaltend ein Material in Form eines schwammartigen Gebildes, das dreidimensionale polymere Netzwerke aufweist und, sofern das Material im Magen und/oder Dünndarm abbaubar ist, mit einer Verbindung versehen ist, die ausschliesslich im Darm löslich ist. Ferner betrifft die vorliegende Erfindung ein Verfahren zur Herstellung eines solchen Mittels sowie dessen Verwendung.

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COMBINED DECLARATION FOR PARENT APPLICATION AND POWER OF ATTORNEY *(includes Reference to PCT International Applications)*	Attorney's Docket No. **FI-37**

As a below named inventor, I hereby declare that:
My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: **AGENT FOR STIMULATING BOWEL FUNCTION AND METHOD FOR PRODUCING THE SAME**

the specification of which (check only one item below):

[ ] is attached hereto.

[ ] was filed as United States application
Serial No. _____
on _____,
and was amended
on _____(if applicable).

[X] was filed as PCT international application
Number **PCT/EP00/08647**
on **September 5, 2000**,
and was amended under PCT Article 19
on _____(if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a). I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. 119:

COUNTRY *(if PCT, indicate PCT)*	APPLICATION NUMBER	DATE OF FILING *(day, month, year)*	PRIORITY CLAIMED UNDER 35 USC 119
GERMANY	**199 42 365.2**	**6 September 1999**	[X] YES [ ] NO
GERMANY	**299 15 634.6**	**6 September 1999**	[X] YES [ ] NO

PTO-1391 (REV. 10-83) U.S. DEPARTMENT OF COMMERCE - Patent and Trademark Office

Combined Declaration For Parent Application and Power of Attorney (Continued) *(includes Reference to PCT International Applications)*	Docket No. **FI-37**

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of the application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty of disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occured between the filing date of the prior application(s) and the national or PCT internation filing date of this application:

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U.S. APPLICATIONS		**STATUS *(CHECK ONE)***		
U.S. APPLICATION NUMBER	U.S. FILING DATE	PATENTED	PENDING	ABANDONED

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POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. *(List name and registration number)*

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Combined Declaration For Parent Application and Power of Attorney (Continued) *(includes Reference to PCT International Applications)*	Docket No. FI-37

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

SIGNATURE OF INVENTOR 201	*SIGNATURE OF INVENTOR 202*	*SIGNATURE OF INVENTOR 203*
DATE 25. Feb. 2002	*DATE*	*DATE*

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